

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

BLK

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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

To:
KEVIN L. BASTIAN
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER, 8TH FLOOR
SAN FRANCISCO, CA 94111

021958-000100PC

Date of mailing
(day/month/year) **28 JUN 2005**

Applicant's or agent's file reference
21958-IPC

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US04/33224

International filing date
(day/month/year) 06 October 2004 (06.10.2004)

Applicant
GANGAGEN, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.
- Filing of amendments and statement under Article 19:**
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):
- When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report. **8/28/05**
- Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35
- For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:**
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. **6/6/05**

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer

Jennifer Dunston

Telephone No. 571-272-1600

J. Roberts for

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

DOCKETED BY ant 19 amendment (optional)

search report rec'd
DOCKETED BY *JH*

DOCKETED BY *8 file IDS in US*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 21958-IPC	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US04/33224	International filing date (<i>day/month/year</i>) 06 October 2004 (06.10.2004)	(Earliest) Priority Date (<i>day/month/year</i>) 06 October 2003 (06.10.2003)
Applicant GANGAGEN, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/33224

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 48/00; C12N 7/00 US CL : 514/44; 424/93.2; 435/235.1 According to International Patent Classification (IPC) or to both national classification and IPC														
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/44; 424/93.2; 435/235.1 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet														
C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>WO 01/79524 A2 (NORRIS et al) 25 October 2001 (25.10.2001), especially pages 1, 18-38, 53-54, 60-65 and 76-78.</td> <td>1-15 and 17-25</td> </tr> <tr> <td>X</td> <td>US 4,695,541 (TAYLOR) 22 September 1987 (22.09.1987), especially column 2 and Example 1.</td> <td>15-16</td> </tr> <tr> <td>A</td> <td>LOPEZ et al. Enzymes for Anti-Infective Therapy: Phage Lysins. Drug Discovery Today: Therapeutic Strategies. December 2004, Vol. 1, No. 4, pages 469-474.</td> <td>1-25</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	WO 01/79524 A2 (NORRIS et al) 25 October 2001 (25.10.2001), especially pages 1, 18-38, 53-54, 60-65 and 76-78.	1-15 and 17-25	X	US 4,695,541 (TAYLOR) 22 September 1987 (22.09.1987), especially column 2 and Example 1.	15-16	A	LOPEZ et al. Enzymes for Anti-Infective Therapy: Phage Lysins. Drug Discovery Today: Therapeutic Strategies. December 2004, Vol. 1, No. 4, pages 469-474.	1-25
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<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.														
<table border="0"> <tr> <td> * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family </td> </tr> </table>			* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family										
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Date of the actual completion of the international search 10 June 2005 (10.06.2005)		Date of mailing of the international search report 28 JUN 2005												
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Jennifer Dunston <i>J. Roberts for</i> Telephone No. 571-272-1600												

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/33224

Continuation of B. FIELDS SEARCHED Item 3:
EAST, MEDLINE, EMBASE, BIOSIS, CAPLUS

keywords: phage therapy, bacteriophage therapy, nonreplicating, escherichia, staphylococcus, pseudomonas, streptococcus, helper
phage, tail

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
KEVIN L. BASTIAN
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER, 8TH FLOOR
SAN FRANCISCO, CA 94111

BLK

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

021958-000100PC

Date of mailing
(day/month/year) 28 JUN 2005

Applicant's or agent's file reference

FOR FURTHER ACTION

See paragraph 2 below

21958-IPC

9/28/05

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US04/33224

06 October 2004 (06.10.2004)

06 October 2003 (06.10.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 48/00; C12N 7/00 and US Cl.: 514/44; 424/93.2; 435/235.1

Applicant

GANGAGEN, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

8/6/05

9/28/05

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Jennifer Dunston

Telephone No. 571-272-1600

J. Roberts for

Form PCT/ISA/237 (cover sheet) (January 2004)

response to written response
DOCKETED BY

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/33224

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/33224

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-25</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-25</u>	NO
Industrial applicability (IA)	Claims <u>1-25</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-15 and 17-25 lack novelty under PCT Article 33(2) as being anticipated by Norris et al. Norris et al teach a method of making a non-replicating anti-bacterial phage that can serve as a molecular vehicle that delivers ribozyme(s) and/or toxic agent(s) to the target cell or pathogen, comprising introducing a transfer plasmid comprising a PAC site into a bacterium comprising a P1 lysogen unable to package its own DNA (e.g. pages 36-37; page 60, lines 20-30). The nucleic acid of the anti-bacterial phage is removed (i.e. substantial deletion), and thus the phage is unable to replicate (e.g. pages 36-37). Norris et al teach the use of a pharmaceutically acceptable complementing host bacterium, such as one comprising a helper phage unable to package its own DNA (e.g. page 38, lines 1-20; page 76, line 35 to page 78, line 15). Norris et al teach a pharmaceutical composition of a non-replicating (i.e. genetically incompetent) anti-bacterial phage (e.g. paragraph bridging pages 53-54; pages 62-65). Further, Norris et al teach the use of said pharmaceutical compositions for the treatment or prophylaxis of bacterial infections in a human subject (e.g. paragraph bridging pages 53-54; page 62, lines 1-6; page 1, lines 7-30). Moreover, Norris et al teach a method of identifying an anti-bacterial phage, comprising making a phage in a host cells, and testing for the ability of the phage to induce cell death in target cells while it does not deliver replicable nucleic acids native to the deliver vehicle pages 32-34, 5.3.1 Biologic Delivery Vehicles; page 36, lines 18-35; page 76).

Claims 15 and 16 lack novelty under PCT Article 33(2) as being anticipated by Taylor et al. Taylor et al teach the isolation of tail protein capable of hydrolyzing alpha 2,8-linked N-acetyl neuraminic acid, comprising replicating phage in a host production bacterium, harvesting said phage and removing substantially all of the nucleic acids through chemical treatment and isolation of the tail protein with the hydrolytic activity (e.g. column 2, lines 41-55; Example 1).

Claims 1-25 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/33224

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: the phrase contained within the brackets on page 37, line 18 appears to have been inadvertently included as part of the disclosure.

Claim 14 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: the claim text contains additional text in the form of a bracketed phrase, which is not part of the claim sentence.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/33224

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 16 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 16 indefinite for the following reason(s): the metes and bounds of the phrase "including a myoviridae or siphoviridae phage" are unclear. It is unclear as to whether these are merely representative phages of the class of tailed phage, or if the phrase intends to further limit the structure of the tailed phage to a tailed phage selected from the group consisting of myoviridae and siphoviridae phage.